PSJ17 Exh 52

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This letter is to inform you of certain compliance issues at Cephalon, Inc. of 145 Brandywine Parkway, West Chester PA. As a former employee responsible for conducting Quality Assurance audits, I am aware of violations for which the company has taken no action. In fact, I believe my employment was terminated for publishing a report within the company detailing non-compliance in at least one of these areas.

As with any company, there are several things that need to be corrected, some more serious and some less. I am aware of several issues but the most important, and the one for which I believe I was terminated regards the Actiq (oral Fentanyl Citrate on a stick) Risk Management Program. This program is a condition of approval in the Actiq NDA detailing several obligations the company has regarding the monitoring and reporting of marketing, prescribing habits, adverse events, pharmacy compliance, and patient education.

I published an internal audit report about 1 December 2003 detailing the points for which the company was not in compliance. I do not have a copy of the report available to me at this time. My recollection of the non-compliance in the report includes, among other things, the following points:

1) The company is required to conduct customer surveys of the top four pharmacies. The survey includes questions for the patient regarding the receipt of a "Welcome Kit". The distribution of this kit to each new patient is required as one of the conditions of approval in the NDA Risk Management Program (RMP). The company is also obligated to determine if patients are receiving the kits. If the company becomes aware that kits are not being distributed, the company is required to take some action to address the problem. These requirements are all listed in the RMP.
   - The company only surveys one pharmacy chain, Walgreen's.
   - The Walgreen's surveys for 2002 indicate that approximately 75% of new patients do not receive welcome kits.
   - The company has taken no action to correct the Walgreen's distribution issue.

2) The company is required to do "Point of Dispensing" monitoring as a condition of approval. Exactly how this is to be done is not described in the RMP but the general idea is that some company representative is expected to spot check pharmacies to verify that they are distributing welcome kits to new patients. If it is determined that kits are not being distributed, the company has an obligation to address the issue.
   - No point of dispensing monitoring is conducted apart from the Walgreen's direct patient call back surveys.
   - Walgreen's surveys indicate that the point of dispensing requirement is not being met.
   - The company has taken no action to correct the point of dispensing issue.

3) The drug is approved for a very narrow therapeutic category. The RMP is designed to assure that the drug is not marketed outside the approved use. The company is required to monitor physician prescribing habits. Physician specialties are described as either representing appropriate patient selection or inappropriate patient selection. If the ratio of prescriptions by specialties representing inappropriate patient selection exceeds 15% of the total prescriptions written, the company is required

to report this to the FDA and required to conduct physician training programs for the offending specialties.

- In one section of the Quarterly Reports to FDA, the company simply states that no individual specialty exceeds 15%. (This statement applies to the three or four specialties designated to represent appropriate patient selection as well as the dozen or more specialties representing inappropriate patient selection.)
- In the section corresponding to the specialties representing appropriate vs. inappropriate patient selection requirement, nothing is reported. This section is routinely omitted from the report.
- Prescribing data is not analyzed by appropriate and inappropriate patient selection so the ratio has not been determined or reported.
- The company has taken no action to reduce the ratio of prescriptions written by specialties representing inappropriate patient selection. (On the contrary, I believe in annual reports and financial statements they tout their ability to grow this drug at an extraordinary rate.)

I believe that Cephalon, Inc. of West Chester, PA would fail an FDA inspection of the Risk Management Program. I believe that Cephalon management knows this and has not taken actions to correct the issues. I believe that my termination was in part, retribution for publishing a document to Cephalon management that stated that Cephalon was not in compliance, and in part, continuing to ask for follow up action.

If I can be of assistance or if you need further information, I can be reached at the above address or at (856) 914-1370.

Kind Regards,
Dave Brennan

Whistle Notes

- RMP Compliance
  - 75% of new Walgreen's patients do not get Welcome Kit. No attempt made to correct.
  - Point of Use compliance requirements not being monitored except via Walgreen's survey.
  - Failure to notify FDA or act to correct significant levels of off-label use.
  - Delays in allowing the audit report to be published.
  - Failure to take action after formal notification.
  - Prevented solicitation of overdue response.

- Actiq content uniformity
  - CU investigation discrepancies re Hulbert's report that not all Mallinckrodt API samples were the same (supported by data) and Akpieta's conclusion to the opposite (with no data to support).
  - Use of erroneous conclusions to justify release of lots.
  - Failure to take any action to correct or investigate when this was verbally communicated to Sheehan.

- Actiq method validation
  - Method has not been demonstrated to be stability indicating. (No specificity studies.)
  - Failure to take any action after formal notification and repeated documented attempts to obtain a response.

- WC QC OOS Investigations
  - Inadequate investigation documentation. Specific examples pointed out in two consecutive annual audit reports. Latest # LI-03-031?
  - Knowingly reported data generated with an invalid procedure (sample prep error at half conc.).
  - Failure to correct systemic problem.

- 2002 Release of "failed" lot
  - Made decision to release while it was believed to not meet unknown impurity spec.
  - Only after decision made to release was it known that unknown peak could be resolved into two peaks, each meeting spec, by altering the method.
  - Released using altered method.